ENVIRONMENTAL TOBACCO SMOKE

Briefing Book

INTRODUCTION

INTRODUCTION

> "The totality of data on ETS and lung cancer does not support the claim made in the draft EPA report that ETS is responsible for an increased incidence of lung cancer in the United States. ... There is no scientifically valid basis for conducting a risk assessment on ETS or classifying ETS as a known carcinogen or even probable human carcinogen."
>
> --Dr. W. Gary Flamm
> Former Assistant Director for Cancer Cause and Prevention, National Cancer Institute and Director for Office of Toxicological Sciences, Food & Drug Administration

Scientifically speaking, environmental tobacco smoke is a combination of (1) highly diluted smoke released from the tip of a burning cigarette and (2) a smaller amount of residual smoke exhaled by the smoker.

Politically speaking, environmental tobacco smoke -- also known as ETS, "secondhand smoke" or "passive smoke" -- is the latest issue in a long line of science vs. social agenda battles in the United States.

Viewpoints range from:

- ETS constitutes a known human, or Group A, carcinogen and should be classified as such by the U.S. Environmental Protection Agency (EPA).

to:

- The available scientific data do not adequately support the conclusion that ETS should be classified as a known human carcinogen, requiring government regulation.

The EPA -- which has the responsibility to make unbiased risk assessments of suspected environmental hazards -- released its draft risk assessment on ETS in June 1990. The draft document, entitled "Health Effects of Passive Smoking: Assessment of Lung Cancer in Adults and Respiratory Disorders in Children," recommended that ETS be classified as a Group A carcinogen.

The Agency's independent Scientific Advisory Board (SAB) Committee on Indoor Air Quality has concurred with the conclusion reached in the EPA draft document, as has the Executive Committee of the SAB.

However, numerous questions have been raised regarding:

- Discrepancies between stated EPA guidelines for performing risk assessments and the procedures used in the draft risk assessment on ETS.

- The EPA's conclusion that an association exists between ETS and lung cancer when, of the 24 studies EPA reviewed on the effects of ETS on non-smokers, 19 reported no statistically significant elevated risk of lung cancer associated with ETS, while those that claimed statistical significance report only a "weak" association. (There are now 30 published studies, 24 of which report no statistical significance.)

- The omission in the EPA draft of several of the largest and most comprehensive studies in their calculations of relative risk.

Concurrent with its release of the draft ETS risk assessment, the EPA also released a draft workplace policy guide recommending ETS be removed from the workplace and public facilities. This guide was based in part on the conclusions reached in the unreviewed draft risk assessment on ETS. This has raised further questions about:

- The propriety of EPA's issuing a policy-oriented workplace guideline based on a draft risk assessment which had yet to be reviewed;

- The propriety of EPA's issuing workplace guidelines that seek to regulate health and safety matters in the workplace, areas under the aegis of Occupational Safety and Health Administration (OSHA), not EPA.

- EPA's ability to separate the scientific risk assessment process from policy issues.

A rigorous review of (1) the process by which EPA conducts carcinogen risk assessments and (2) the available science on ETS raises serious concerns of interpretation and procedures:

- Does the available science support the classification of ETS as a Group A carcinogen?
- Has the EPA followed its own guidelines to ensure an unbiased risk assessment with respect to ETS?
- Is the EPA's agenda social and political, rather than scientific, with respect to ETS?
- Is the EPA's entire risk assessment process in need of revision?

The purpose of Part I of this book is to provide a clear, concise picture of the science on ETS and the EPA's risk assessment process.

Part II provides an overview of the status of indoor air quality research and the role of ventilation in addressing the problem of indoor air quality, often wrongly attributed to ETS.

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PART I

BACKGROUND ON ETS

"What really is ETS? In comparison to mainstream smoke and sidestream smoke, ETS is so highly diluted that it is not even appropriate to call it smoke, in the conventional sense. Indeed, the term 'Environmental Tobacco Smoke' is a misnomer."

-- Gary L. Huber, MD; Robert E. Brockie, MD and Vijay K. Mahajan, MD
"Passive Smoking: How Great a Hazard?"
Consumers' Research, July 1991

ETS is not mainstream or sidestream tobacco smoke.

- Mainstream smoke: tobacco smoke drawn through the butt end of the cigarette and inhaled by a smoker during active smoking.
- Sidestream smoke: tobacco smoke released from the smoldering tip between puffs.
- Environmental tobacco smoke: a combination of highly diluted sidestream smoke plus a smaller amount of residual mainstream smoke exhaled by the active smoker.
- ETS consists of only a limited number of identified "remnants" or "residual constituents" of sidestream and mainstream smoke in highly dilute concentrations, but is chemically and dynamically different from both. It often is improperly equated with or attributed with the characteristics of one or both.
- Only a fraction of the constituents of mainstream smoke and sidestream smoke have been identified in ETS, most of which occur normally in indoor air and are not necessarily indicators of the presence of ETS.
- ETS is constantly changing in nature due to numerous environmental and personal factors, so there is no defined, reproducibly characterized entity known as ETS.
- Due to the changing nature of ETS, scientists have been unable to locate a specific chemical or compound that consistently or reliably indicates the presence of ETS entirely in the air or internally in non-smokers (markers). In epidemiologic studies, exposure is measured indirectly -- generally through reports of spousal smoking habits. The degree of actual nonsmoker exposure is unknown.

- In a 1989 report to Congress, EPA acknowledged the difference between ETS, mainstream smoke and sidestream smoke, and identified areas of research critical to the determination of health risks from ETS. These research areas included:

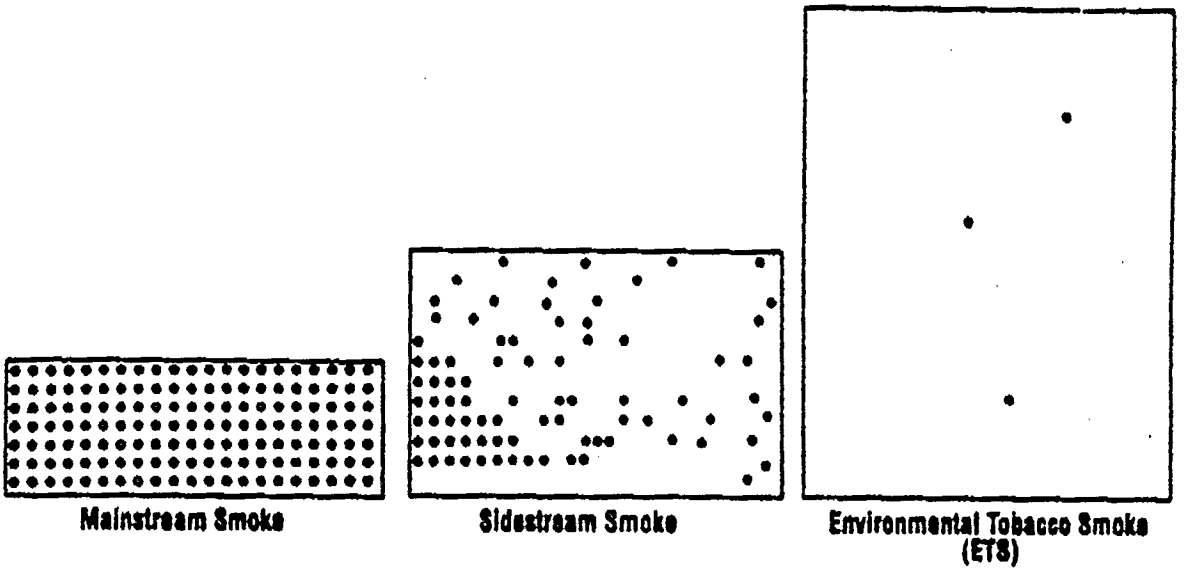
  (1) identification and characterization of toxicologically significant components in ETS;

  (2) determination of the distribution of ETS ingredients in the particulate and vapor phases; and

  (3) identification and evaluation of markers for these phases.

  These questions, which are necessary to satisfy at least two components of the ETS risk assessment process, remain unanswered.

Figure 1: **Particulate Phase and Gas Phase of Tobacco Smoke***



* Schematic representation of the particulate phase and the gas phase of tobacco smoke. Environmental tobacco smoke is not smoke in the conventional sense, but rather a very limited number of highly-diluted remnants or residual constituents of mainstream smoke and sidestream smoke.

(Source: Huber et al., "Passive Smoking: How Great a Hazard?", Consumers' Research, July 1991)

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ETS: Annoyance or legitimate cause of disease?

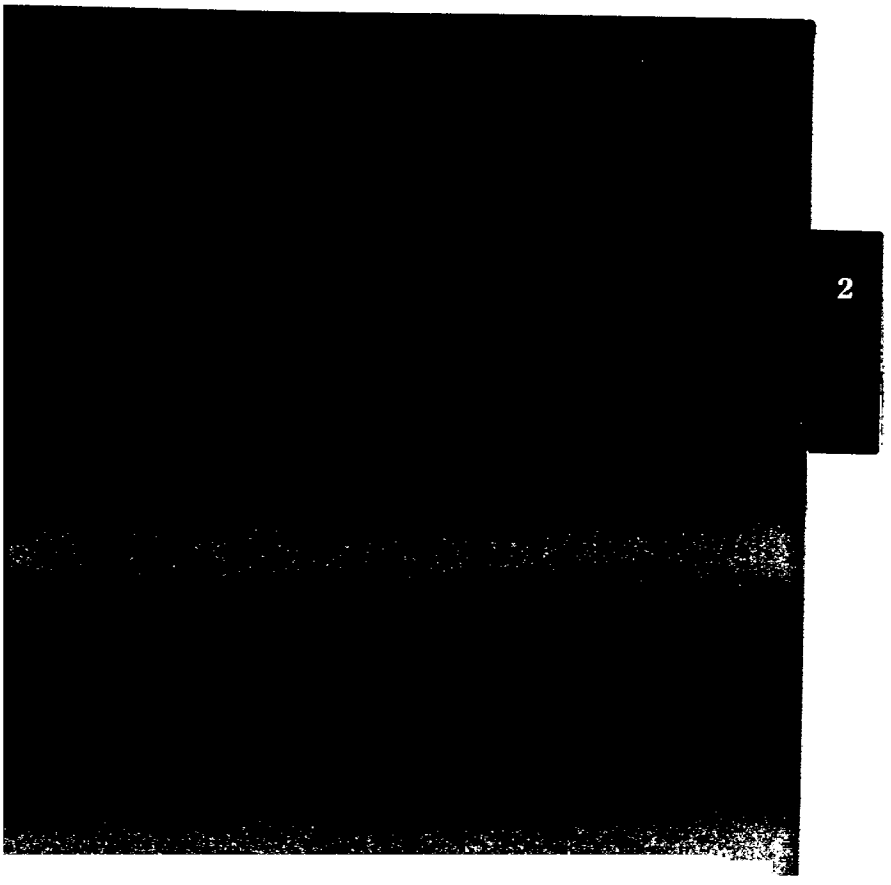
> "The possibility of cancer from secondhand smoke is 'a small added risk, probably much less than you took to get here through Washington traffic.'"
>
> --Dr. Morton Lippman, chairman of SAB indoor air quality committee that reviewed ETS risk assessment, quoted at a press conference announcing the SAB recommendation that ETS be classified a Group A carcinogen.

ETS is viewed by some to be offensive or annoying. However, actual measurements of ETS constituents taken in offices, workplaces and public places indicate that probable exposure of non-smokers to ETS in a variety of public places is minimal.

- "The average person exposed to ETS would retain an annual dose analogous to the active mainstream smoking of considerably less than one cigarette dispersed over a 1-year period." (Gori and Mantel, "Mainstream and Environmental Tobacco Smoke," Regulatory Toxicology and Pharmacology, 1991)

- Based on average smoke concentrations in typical indoor public places (e.g., commuter vehicles, restaurants, cocktail lounges), the average person would be exposed to the equivalent of 1/1000 to 9/1000 of one filter cigarette per hour.

  In other words, a person would have to spend up to 1,000 hours in public places to be exposed to the equivalent of one filter cigarette. (Hinds and First, "Concentrations of Nicotine and Tobacco Smoke in Public Places," The New England Journal of Medicine, April 1975).



SCIENCE BEHIND ETS

Measuring possible disease risks of ETS.

"New rules should not be 'made to fit' an otherwise unproved hypotheses, just because the subject is tobacco and the observed results do not support the hypothesis investigated."

--Gary L. Huber, MD, Robert E. Brockie, MD, and Vijay K. Mahajan, MD.
"Passive Smoking: How Great a Hazard?"
Consumers' Research, July 1991

"In the case of ETS it would be unfortunate if potentially irresolvable scientific uncertainties thwarted control."

--Dr. Jonathan Samet, member of EPA review panel for ETS, "The Environment and the Lung," Journal of the American Medical Association, August 7, 1991

Two different approaches generally have been used to assess indirectly the possible disease risks for non-smoker exposure to ETS.

o Linear Risk Extrapolation

"Because of the physiochemical nature of ETS, mainstream smoke and sidestream smoke differ, the extrapolation of health effects from studies of mainstream smoke of active smokers to nonsmokers exposed to ETS may not be appropriate."

--National Academy of Sciences

-- Concept. Mathematical theory that assumes that if there is a definable disease risk for the active smoker, then a lesser risk exists for a non-smoker exposed to ETS, which can be projected directly or "linearly".

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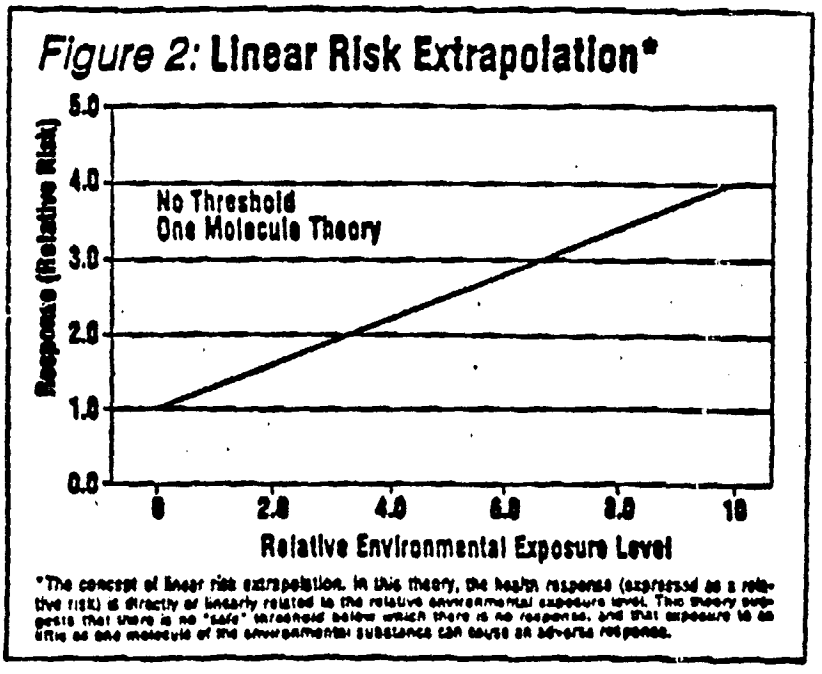

(Chart source: Huber et al., Consumers' Research, July 1991)

-- Limitations. For this theory to be valid, at least the following assumptions must be true:

- o Risk applies to all exposure levels, no matter how low -- even one molecule.
- o Exposed individual has no capacity to adapt to the exposure.
- o The potential for risk from exposure to the agent under consideration is independent of any confounding factors, i.e., other lifestyle factors that may create the appearance of an association between the agent and lung cancer where none exists (e.g., diet, alcohol consumption, occupational exposures).
- o Risk is linear for duration of exposure and is linear for concentration of exposure.

None of these assumptions has been proven for comparative projections of mainstream smoke to ETS. There presently is no clear way to evaluate or compare levels of exposure in active smokers with non-smokers exposed to ETS. (See Huber et al.).

o Epidemiologic Studies

"Because of the methodologic difficulties of assessing lifetime exposure to environmental tobacco smoke and precisely describing risks that are not substantially elevated, these uncertainties in assessing the lung cancer risk of [ETS] may never be fully resolved, although they remain a subject of research."

--Jonathan M. Samet, MD and Mark J. Utell, MD, "The Environment and the Lung," Journal of the American Medical Association, 8/7/91.

-- Concept. Use of epidemiology, a branch of medical science that studies the distribution of disease in human populations and the factors determining that distribution, chiefly through statistics.

The bases for epidemiologic studies on ETS have been disease rates in non-smokers living with a spouse who smokes.

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-- Limitations. Epidemiologic studies on ETS are flawed due to their inability to assess a well-defined exposure.

- Because ETS exposure levels cannot be measured or quantified directly, epidemiologists have had to use indirect estimates ("surrogates") of ETS exposure.

- Estimates of ETS exposure based on spousal or parental smoking have been derived through questionnaires; no study employs any direct quantification of ETS or ETS remnant constituents in the actual environment of the nonsmoker.

- Studies are subject to:

  --Misclassification bias: bias caused by misclassification of some current or former smokers as non-smokers.

  --Recall bias: mistaken recall by questionnaire interviewee on smoking history of the case, the control or the spouse.

  --Confounding variables: Lifestyle factors that may create the appearance of an association between ETS and lung cancer where none exists (e.g., cultural differences, diet, alcohol consumption, occupational exposures).

Review of Epidemiologic Data on ETS

> "If war is too important to be left to military leaders, and medicine to physicians, the interpretation of epidemiologic results cannot be relegated exclusively to epidemiologists. The people who struggle to understand those results can be helped by recalling the old adage that statistics are like a bikini bathing suit: what is revealed is interesting; what is concealed is crucial."
>
> --Dr. Alvan R. Feinstein, director, Clinical Epidemiology Unit, Yale University, "Scientific Standards in Epidemiologic Studies of the Menace of Daily Life," Science, December 1988.

Thirty epidemiologic studies have been published on lung cancer and spousal smoking. All are based on the concept of relative risk, which is a statistical measure of the association between a substance and an effect.

Relative risk: A value derived by dividing the incidence of lung cancer in the so-called ETS-exposed group by the incidence of lung cancer in the nonexposed group.

$$\frac{\text{Rate of lung cancer in ETS-exposed group}}{\text{Rate of lung cancer in non-exposed group}} = \text{Relative risk}$$

(e.g., $\frac{10}{10} = 1.0$ relative risk)

If the disease rates were identical in these two groups, the risk ratio would be 1.0, meaning that there was no indicated increased risk of lung cancer among non-smokers who report exposure to ETS.

Relative risk is either strong or weak, depending on the degree of association or the magnitude of the risk ratio. Epidemiologic studies are more meaningful when the association is strong, i.e., shows a high relative risk.

The generally accepted measure of weak relative risk is the range of 1 to 3 or so.

At this level, a reported finding of risk may be artifactual and due to problems in case-study selection, and/or the presence of other variables and interpretation biases that can influence the outcome of a study.

Epidemiologic studies do have significant limitations since they are limited to observational effects on large populations where precise control of many other factors is not possible, and they usually are based on questionnaires that rely on respondent recall.

Because of these limitations, epidemiologic studies can be significantly influenced by chance, bias or confounding factors. The weaker the association (small relative risk) the greater the chance that these other factors had an impact on the outcome.

Published Studies of ETS and Lung Cancer in Non-smokers

Study	Sex	No. of Cases	Relative Risk
Case Control Studies:			
Chan and Fung, 1982	F	34	0.75
Trichopoulos et al., 1983	F	38	2.13*
Correa et al., 1983	F	14	2.07
	M	2	1.97
Kabat and Wynder, 1984	F	13	0.79
	M	5	1.00
Buffler et al., 1984	F	33	0.80
	M	5	0.51
Garfinkel et al., 1985	F	92	1.12
Wu et al., 1985	F	29	1.20
Akiba et al., 1986	F	73	1.52
	M	3	2.10
Lee et al., 1986	F	22	1.03
	M	8	1.31
Brownson et al., 1987	F	19	1.68
Gao et al., 1987	F	189	1.19
Humble et al., 1987	F	14	1.78
Koo et al., 1987	F	51	1.55
Lam et al., 1987	F	115	1.65*
Pershagen et al., 1987	F	33	1.20
Geng et al., 1988	F	34	2.16*
Inoue and Hirayama, 1988	F	18	2.55
Katada et al., 1988	F	17	
Lam and Cheng, 1988	F	37	2.01*
Shimizu et al., 1988	F	90	1.10*
He, 1990	F	45	0.74
Janerich et al., 1990	F	129	0.93
Kabat, 1990	M	13	1.20
	F	35	0.90
Kalandidi et al., 1990	F	91	2.11
Sobue et al., 1990	F	64	0.94
Svensson, 1990	F	17	1.20
Wu-Williams et al., 1990	F	205	0.70
Cohort Studies:			
Garfinkel, 1981	F	88	1.17
Gillis et al., 1984	F	6	1.00
	M	4	3.25
Hirayama, 1984b	F	163	1.45
1984a		7	2.28*

Note: Weak relative risks have risk ratios of between 1 and 3, or so. Any risk ratio below 1 represents a negative relationship. Note that all of the studies show a weak relative risk.

*Findings are statistically significant at the 5% level, i.e., there is a 95% probability that results are not attributable to chance.

(Source: Huber et al., Consumers' Research)

Description of Epidemiologic Studies

"Some epidemiologic studies of nonsmokers presumably exposed to ETS have suggested a marginal increase of risk for some diseases previously associated with active mainstream smoking. These reported risks, however, border on statistical and epidemiologic insignificance, and could easily derive from numerous and documented biases and confounders."

--Gio Batta Gori and Nathan Mantel, "Mainstream and Environmental Tobacco Smoke," Regulatory Toxicology and Pharmacology, 1991

- 30 epidemiologic studies have been published on ETS and lung cancer.
- 24 report no statistically significant association between lung cancer and exposure to ETS.
- The 6 studies reporting statistical significance fall in the weak category of relative risk, that is, between 1.0 and 3.0.
- The 6 studies on spousal smoking purporting to show statistical significance were conducted on non-U.S. (primarily Asian) populations; confounders such as dietary and other lifestyle habits that may have affected the results were not taken into consideration adequately.
- One of the largest studies on this subject (Wu-Williams), released December 1990, reported non-smoking spouses of smokers actually had less risk of developing cancer than non-smokers married to other non-smokers, and it took into account other lifestyle factors.
- Two additional Asian studies published around the same time (Sobue and He) also reported no statistically significant risk for lung cancer in non-smoking women married to smokers.
- All three of these recent Asian studies adjusted for cultural differences. They reported that Asian cooking and heating techniques posed an increased risk for the development of lung cancer among non-smoking women, independent of reported ETS exposures.

- Some of the studies that purported to show increased relative risk considered only a few subjects. The preponderance of study participants were wives exposed to ETS through smoking husbands.

- The Hirayama study, considered the EPA's "flagship" study, has been criticized by other scientists as being substantially flawed. When asked to respond to criticism, Hirayama could not or would not produce his raw data; he claimed it had been destroyed.

Comparison of Reported ETS Relative Risk with Reported Relative Risks of Other Factors Linked to Lung Cancer

For comparative purposes, the following table lists some examples of relative risks for independent factors reported as related to lung cancer risk.

Reported Independent Risk Factors for Lung Cancer

Factor	Reference	Max. Relative Risk Reported
Family history of lung cancer	Samet et al.(1986)	5.3
	Ooi et al.(1986)	2.4
	Horwitz et al.(1988)	2.8
	Wu et al.(1988)	3.9
Family history of tuberculosis	Wu et al.(1988)	10.0
	Sakurai et al.(1989)	6.4
	Hinds et al.(1982)	8.2
Alcohol intake	Pollack et al.(1984)	2.19
Dietary fat intake	Wynder et al.(1987)	4-6
Pork meat intake	Mettlin(1989)	2.4
Milk intake	Mettlin(1989); Mettlin et al. (1990)	2.1
Cooking methods	Gao et al.(1987)	1.4-2.6
	Geng et al.(1988)	5.6
	Sobue et al.(1990)	1.9
	Mumford et al.(1987)	2-3
Radon	Edlin et al.(1984)	4.3
Occupation	Kvale et al.(1986)	2.6
Motor exhaust exposure	Hayes et al.(1989)	1.5
Socioeconomic class	Brown et al.(1975)	2.6-3.8
Ventilatory function	Lange et al.(1990)	2-4
Physical inactivity	Albanes et al.(1989)	1.6
Urban/rural risk ratio	Shy(1984)	1.2-2.8

(Source: Gori and Mantel, "Mainstream and Environmental Tobacco Smoke," Regulatory Toxicology and Pharmacology, 1991)

Review of Animal Data on ETS

In addition to epidemiologic studies, two animal inhalation studies also have been published which investigate ETS and lung cancer.

Both studies report no meaningful differences in tumor incidence between animals exposed to ETS and those not exposed.

- Study One: One group of hamsters was exposed to mainstream smoke and another group to ETS.
  - -- Animals exposed to mainstream smoke and ETS lived longer than the control group.
  - -- Investigators reported that overall there was no marked increased in tumor incidence in animals exposed to either mainstream smoke or ETS after 18 months of exposure.

  (American Health Foundation, Haley, N., "Uptake of Sidestream Smoke by Syrian Golden Hamsters")

- Study Two: Rats and hamsters were exposed to ETS concentrations 100 times greater than those concentrations typically encountered by non-smokers in a 90-day inhalation study.
  - -- Investigators reported no differences in tissue between exposed and control animals.
  - -- Electron microscopy revealed pulmonary changes which could be expected to occur under similar exposure conditions with other substances.

  (Adlkofer, F., et al., "Exposure of Hamsters and Rats to Sidestream Smoke of Cigarettes: Preliminary Results of 90-day Inhalation Study")

In addition, recent reviews of literature on suspected pulmonary carcinogens have indicated that none of the individual constituents in sidestream smoke classified as "potentially carcinogenic" has been found to induce pulmonary cancer via inhalation in experimental animals.

Meta-Analysis

> "To some people, it seems like little more than an attempt by statisticians to put themselves on the top of the totem pole. Individual researchers with their individual experiments see themselves reduced to becoming a cog in the great statistical wheel. And they're saying, well, no, that's not how science works."
>
> --Richard Kronmal, biostatistician, University of Washington, "Meta-Analysis in the Breech," Science, 8/3/90

Concept: A statistical technique for combining similar studies into a single, quantitative analysis. When individual studies show a weak association, statisticians use meta-analysis to increase the ability to statistically detect an association, if such an association is present.

The EPA used meta-analysis in its draft risk assessment on ETS, pooling selected epidemiological studies to arrive at a single estimate of relative risk of 1.28.

Limitations:

- Meta-analysis is only as good as the available studies. Because meta-analysis utilizes studies already published, the results will depend on whether or not the available studies have been well-designed, well-executed and interpreted.

- Accounting for bias. If the meta-analyst does not correct for biases inherent in the individual studies being combined, the resulting meta-analysis may reflect an artificially increased relative risk.

- Bias in favor of positive results. Negative studies (showing no association) are less likely to be published than positive ones; unless a meta-analyst looks for or uses negative studies, there can be a bias in favor of a positive association.

ETS Meta-Analysis by the EPA

> "Biases due to confounding or due to misclassification will not average out when we accumulate evidence across different studies. They will reinforce one another."
>
> --Dr. Joseph Fleiss, Columbia University School of Public Health

o By definition, meta-analysis is the combining of similar studies. The methodology of the individual ETS epidemiologic studies is not consistent; therefore, the appropriateness of EPA applying meta-analysis in its ETS risk assessment is highly questionable.

o The EPA meta-analysis failed to account for many biases and confounders in underlying studies likely to contribute to an artificially increased relative risk.

o The EPA meta-analysis combined both U.S. and non-U.S. studies, resulting in a relative risk assignment of 1.28. EPA is trying to determine health risks to U.S. populations, so studies should have been limited to those relevant to the United States. A meta-analysis of U.S. studies alone reports a relative risk of 1.08.

o The EPA meta-analysis excluded several important studies, including the largest case-control study ever conducted in the United States, and several reporting no statistically significant association between marriage to a smoker and risk of lung cancer.

Additionally, a recent meta-analysis of the available ETS epidemiologic studies by a statistical consultant (Layard Associates, September 1991) reported a relative risk of only 1.04, which is not statistically significant. This meta-analysis:

- Used the same methodology as the EPA in its draft risk assessment;
- Included the most recent published studies, as well as several excluded by the EPA; and
- Adjusted for misclassification bias.

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THE EPA RISK ASSESSMENT PROCESS

Process Overview

> "In putting together panels, we try to find people who are knowledgeable but not too tightly involved and stay away from people who have taken publicly identified positions" on the subject matter.
>
> Mr. Don Barnes, director of EPA Scientific Advisory Board, in describing the process by which the SAB chooses panel members. (The New York Times, 10/21/90)

The risk assessment review process is subject to the following EPA guidelines:

- EPA prepares assessment in "final" draft

- Draft submitted to EPA's independent Science Advisory Board ("SAB") for review.
  --SAB executive committee ("EC") consists of at least 9 members (presently, more than 60 members appointed by EPA Administrator)
  --Divided into Executive Committee and 8 standing committees
  --Members should be independent and highly qualified
  --Additional scientists and engineers may serve as consultants (presently more than 250)
  --EC appoints members to committees and coordinates scientific reviews

- SAB EC selects standing committee to review draft; additional consultants may be added to aid in review

- Review process subject to regulations meant to ensure public access to process and information
  --advance notice of all meetings
  --must vote to close meetings
  --written explanation of decisions to close meetings
  --maintenance of closing-meeting transcripts that can be obtained by public, unless information is exempt
  --SAB open meetings announced in Fed. Reg. several weeks prior to meetings.

- If after review process, SAB standing committee approves draft, it is forwarded to EC for approval.

- If EC approves draft, it is forwarded to EPA Administrator for action. SAB approval is advisory only; not binding on Administrator.

- EPA Administrator takes action.

EPA

Prepares "final" draft position paper

forwards to

↓

Science Advisory Board (SAB) Executive Committee
(EPA's independent board of scientists and engineers)

assigns to

↓

SAB Standing Committee responsible for that issue

- o reviews document
- o publishes notice of meetings and review
- o takes public comments
- o holds meetings
- o makes determination*

forwards to

↓

SAB Executive Committee

- o reviews comments
- o makes determination* and non-binding recommendation to EPA Administrator

forwards to

↓

EPA Administrator

- o reviews comments
- o makes determination of appropriate final disposition

* SAB standing committee or SAB EC may recommend revisions to documents and re-review before forwarding to next appropriate group or person.

Chronology of Events

- Spring 1990. A consultant for EPA's Office of Health and Environmental Assessment (OHEA) prepares preliminary draft document on health risks associated with ETS. The draft advocates classification of ETS as Group A ("known human") carcinogen.

- May 1990. Draft document circulated within EPA for review and "leaked" to press, prior to release to public. Additionally, EPA issues a press release and allows press interviews concerning the draft report's conclusions prior to issuance of the draft to public and members of industry who would be directly affected by regulation of ETS.

- June 25, 1990. EPA releases draft risk assessment and publishes notice of EPA public comment period and indication of referral to Science Advisory Board in the Federal Register.

  Concurrently, EPA releases draft workplace policy guide that addressed health issues, including ETS. The guide recommended policy before the scientific basis of the risk assessment, on which guide is based, had been reviewed.

- June/July 1990. Draft documents assigned to the Indoor Air Quality Committee (IAQC) of the EPA's Science Advisory Board (SAB) for review. SAB Executive Chairman appoints additional committee members. Committee selection creates controversy as members are variously alleged to have links to either anti-smoking groups or the tobacco industry; however, none appointed to the committee had stated opposition to conclusion of initial draft.

- November 20, 1990. Notice of public meetings to be held December 4 and 5 published in Federal Register.

- December 4-5, 1990. IAQC holds open meeting to review draft documents and formally receive written and oral comments from interested parties to aid committee in its independent review process.

- December 5, 1990. Chairman of the committee calls press conference and states that the panel has reached a consensus on the classification of ETS as a known human carcinogen, although he states he is speaking for himself and despite the fact that several panel members have missed parts of the hearing, some panel members have not had a chance to review the public record, and some

members have expressed major criticisms of the drafts at the meeting.

Hearing is completed. The draft report of the SAB committee is sent to SAB Executive Committee for review.

- o April 18, 1991. Executive Committee officially concurs with EPA draft risk assessment that ETS should be classified as a Group A carcinogen.

- o April 23, 1991. SAB finalizes committee report and issues it to EPA Administrator. Reportedly, both the EPA risk assessment and the workplace policy guide will undergo revisions by EPA.

Comparison of Review Process for Diesel Emissions, Electro-magnetic fields and ETS.

The EPA released draft reports for diesel emissions, electro-magnetic fields (EMF) and ETS within 90 days of each other. The following is a comparison of the review process for the 3 substances.

Diesel emissions	EMF	ETS
Publication of draft		
EPA published notice in Fed. Reg. Covers data published since 1983 assessment.	EPA published notice in Fed. Reg.	EPA published notice in Fed. Reg. Conclusions of draft leaked to press prior to publication.
Selection of "Independent, Highly Qualified" Reviewing Committee		
	New group, rather than standing committee, selected from SAB, EPA program offices, interested groups and candidates responding to announcements placed in journals.	Standing Indoor Air Quality committee selected by SAB, augmented by consultants selected from SAB, EPA program offices and interested groups.
Committee Composition		
	Committee members described by EPA as balanced in terms of viewpoints. Not required to disclose relevant ties.	Committee appointments caused great controversy -- allegations of financial ties to both anti-smoking groups and tobacco industry; however, none appointed to committee had stated opposition to initial draft conclusion. There were some calls for disbanding committee.

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Diesel emissions	EMF	ETS
Public Meetings		
Expert science workshop held. Invited participants included experts from universities, gov't labs, regulated motor vehicle industry & public interest groups.	Committee held expert science workshop for public to observe issues as they were debated.	No workshop.
	3 open meetings held for further review of risk assessment by scientific committees.	Only one open meeting held. On 2nd day, chairman announced consensus had been reached by committee, though several members had not reviewed public record, and several had missed part of the meeting.
At least 30 days' notice of meeting.	At least 30 days' notice of each meeting.	12 days' notice of meeting. Two working days' notice to inform committee of intent to appear and make presentation.
	Extensive interaction among committee members scientists & public. Focus on issues.	Very limited interaction among members, scientists & public. Focus on committee members' views.
	All interested parties allowed to present.	Certain scientists presenting viewpoints critical of the draft denied opportunity to present.
Report preparation		
	(3) meetings before report preparation. Writing assignments made available to public.	One meeting before report preparation. Writing assignments not made available to public.

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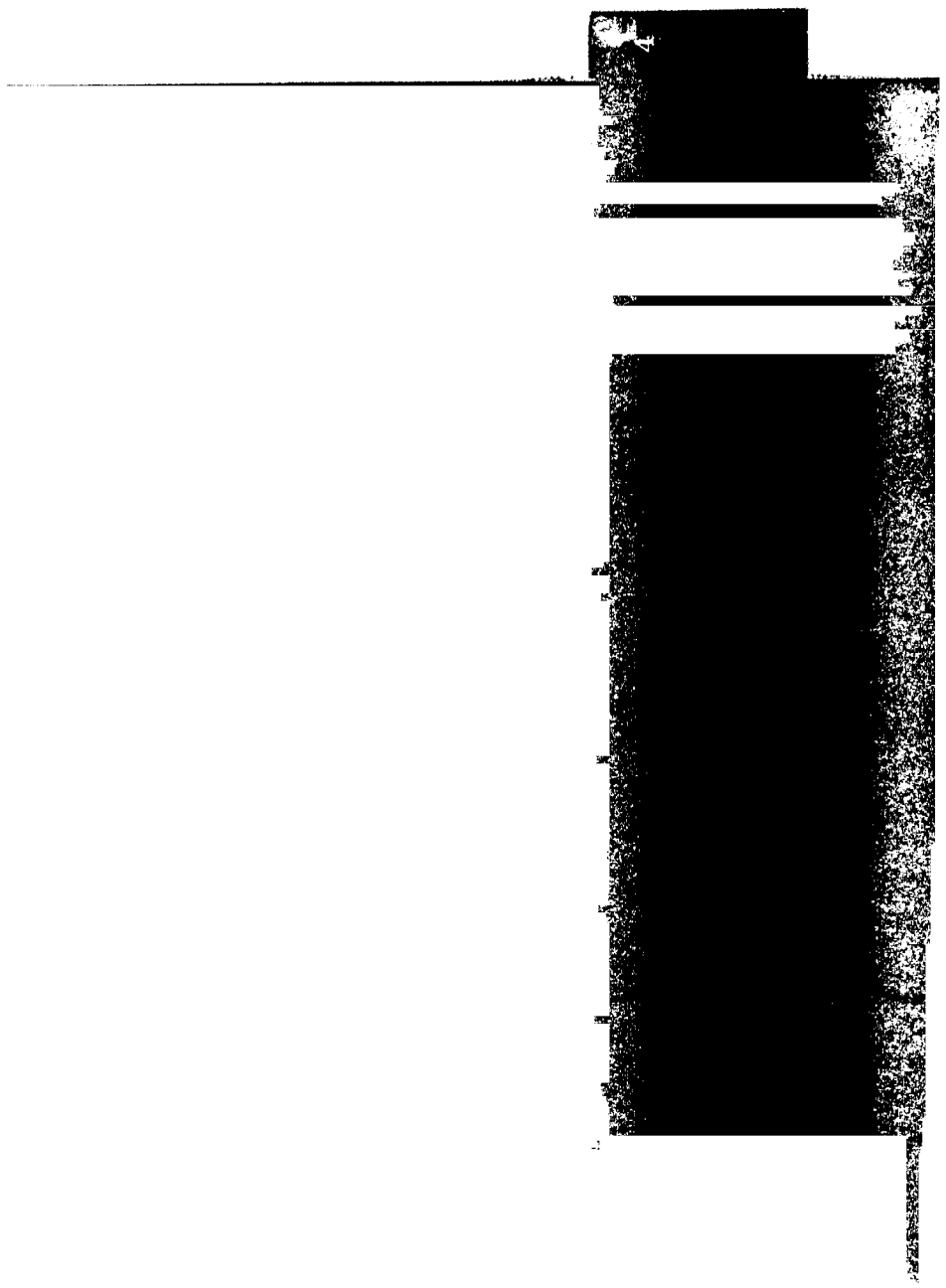
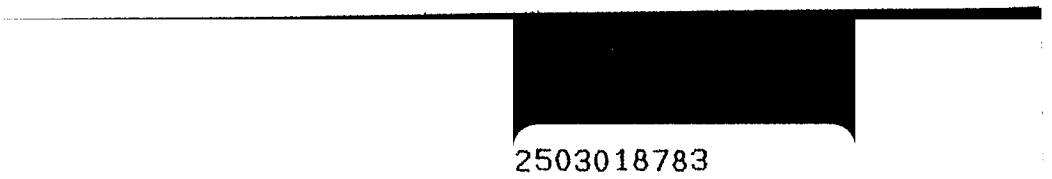
Diesel emissions	EMF	ETS
	Documents and committee deliberations during conference calls made available to public.	Documents and committee deliberations during conference calls not made available to public
Present Status		
	Document undergoing substantial revision before commencement of official public comment period. Document also reviewed by special White House committee established to ensure accuracy of report. Document found to be severely flawed.	Document undergoing revision; will be sent to Administrator for final determination.





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RISK ASSESSMENT GUIDELINES

"Risk assessment ... must be based on scientific evidence and scientific consensus only. Nothing will erode public confidence faster than the suspicion that policy considerations have been allowed to influence the assessment of risk."

--William D. Ruckelshaus, Former EPA Administrator

Overview

In 1986, the EPA issued guidelines for carcinogen risk assessment. The guidelines emphasized:

- full consideration of all relevant scientific information;
- full presentation of scientific information in agency risk assessment documents;
- identification of strengths and weaknesses of each assessment, e.g., uncertainties, assumptions, limitations, and scientific basis and rationale for each assessment.

Risk Assessment Components

According to the 1986 guidelines, risk assessments are comprised of one or more of the following four components:

- Hazard identification -- assessment of relevant chemical and biological information to determine whether a particular substance is causally linked to specific health effects (i.e., whether ETS is causally linked to lung cancer);
- Dose-response assessment -- assessment to determine the the relationship, if any, between the amount of exposure to the substance and the probability of occurrence of the specific health effects;
- Exposure assessment -- assessment to determine the extent to which humans are exposed to the substance;
- Risk characterization -- estimate of the incidence of a health effect under the various conditions described in the exposure assessment. Presents a framework to help judge the significance of the risk.

Assessment and Categorization of Weight of Evidence for Carcinogenicity

Once the EPA has reviewed all relevant information, it utilizes what is known as the overall "weight-of-evidence" approach of evaluating potential risks.

This approach has been described as placing all of the epidemiologic and animal evidence and arguments favoring a positive association on one side of the scales, with all of the evidence supporting the contrary conclusion on the opposite side.

According to the EPA guidelines, three criteria must be met for epidemiologic studies before an association can be inferred between exposure and cancer in humans:

1. There is no identified bias that could explain the association.

2. The possibility of confounding has been considered and ruled out as explaining the association.

3. The association is unlikely to be due to chance.

Evaluation of all these components results in a classification of the suspected carcinogen in one of five groups:

- Group A -- Carcinogenic to humans
- Group B -- Probably carcinogenic to humans
- Group C -- Possibly carcinogenic to humans
- Group D -- Not classifiable as to human carcinogenicity
- Group E -- Evidence of non-carcinogenicity for humans

The following table illustrates the carcinogen classification system of the EPA based on data reviewed. The EPA uses this table as a guide in determining classification based on the level of animal and human evidence available.

Categorization of Evidence

Human Evidence	Animal Evidence				
	Sufficient	Limited	Inadequate	No Data	No Evidence
Sufficient	A	A	A	A	A
Limited	B1	B1	B1	B1	B1
Inadequate	B2	C	D	D	D
No Data	B2	C	D	D	E
No Evidence	B2	C	D	D	E

Categorizations listed in the table may be influenced by relevant animal and human data, and relevant ancillary evidence.

A classification of Group A may be made with no animal test evidence -- providing there is compelling epidemiologic data.

The EPA did not consider the available animal test data in its ETS risk assessment. Since the EPA recommended a classification of Group A for ETS, reference to the classification table indicates that the EPA determined the epidemiologic evidence was sufficient in and of itself to warrant such a classification.

ETS would be the first substance ever classified under Group A based solely on "weak" epidemiologic data.

Present Group A Carcinogens vs. ETS

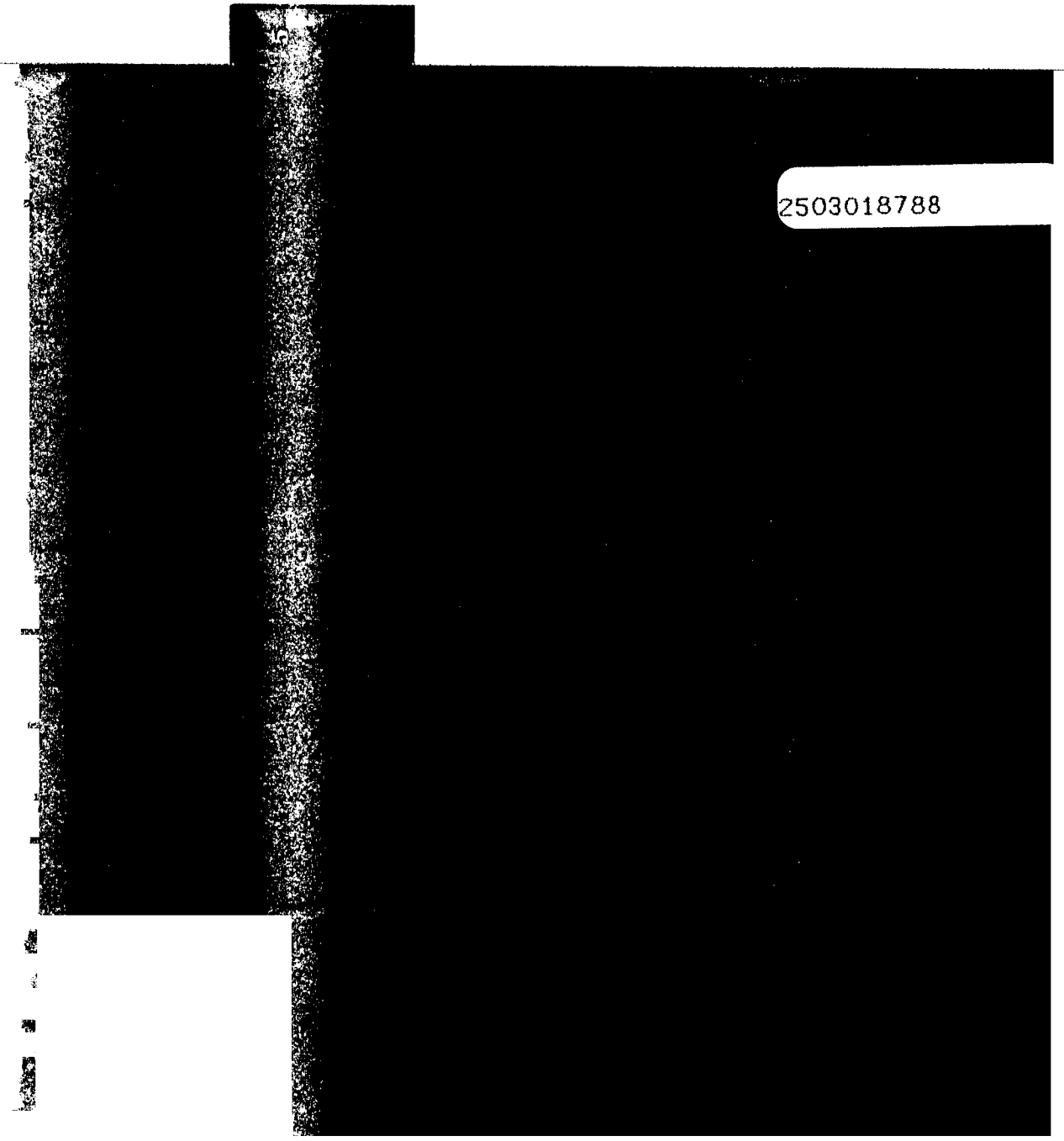
- The EPA has listed only 14 substances or mixtures of substances as Group A carcinogens.
- The data for each of these substances is "clear-cut and unequivocal."
- Relative risks are far higher than those reported for ETS.
- Corroborating animal data is available.
- If ETS were listed as a Group A carcinogen, it would be the first time EPA has listed a complex mixture as such simply because it might contain constituents that are themselves Group A carcinogens (e.g., alpha-napthylamine was not listed as a Group A carcinogen even though it was known to contain beta-napthylamine, a Group A carcinogen).

(Source: W. Gary Flamm, PhD, "Review of the Draft EPA Document Entitled "Health Effects of Passive Smoking; Assessment of Lung Cancer in Adults and Respiratory Disorders in Children," November 1990)

The following table lists relevant data considered by the EPA in its risk assessment of ETS compared with other substances that have been classified as Group A carcinogens.

Substance	Data Considered by EPA in Risk Assessment Process	
	Epidemiologic (Strong/Weak)	Animal
bis (chloromethyl) ether	Yes/Strong	Yes
mustard gas	Yes/Strong	Yes
asbestos fibers	Yes/Strong	Yes
arsenicals	Yes/Strong	Yes
chromium compounds	Yes/Strong	Yes
nickel refining emissions	Yes/Strong	Yes
coke oven emissions	Yes/Strong	Yes
4-Aminobiphenyl	Yes/Strong	Yes
Benzene	Yes/Strong	Yes
Benzidine	Yes/Strong	Yes
2-Naphthylamine	Yes/Strong	Yes
Vinyl chloride	Yes/Strong	Yes
ETS	Yes/Weak	No

(Source: Domingo M. Aviado, MD, "Non-Epdiemiologic Studies on Potential Pulmonary Carcinogens in Environmental Tobacco Smoke: A Critique of the Environmental Protection Agency's Designation of Environmental Tobacco Smoke as a Group A Carcinogen," September 25, 1990)



APPLICATION OF RISK ASSESSMENT GUIDELINES

> "The purpose of the guidelines is to promote quality and consistency of carcinogen risk assessment within the EPA and to inform those outside the EPA about its approach to carcinogen risk assessment."
>
> --51 FR 33993

The following is a comparison of EPA risk assessment evaluations of 3 exposures: diesel emissions, electromagnetic fields (EMF) and ETS.

EPA GUIDELINES	Diesel Emissions	EMF	ETS
Hazard Identification			
a. Physical-Chemical	Addressed		Not Addressed Literature on ETS composition not discussed. One table for mainstream v. sidestream smoke.
b. Metabolism and Pharmacokinetic	Addressed	Addressed	Not addressed. No reference to or assessment of relevant analytic literature.
c. Toxicologic effects	Addressed Toxic effects reported in some animal studies suggest that it is pulmonary carcinogen among rodents exposed to large doses by inhalation.	Addressed	Not addressed. Omission of 2 subchronic animal inhalation studies showing no tumorigenic effect from ETS exposure.

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EPA GUIDELINES	Diesel Emissions	EMF	ETS
d. Short-term tests	Addressed	Addressed	Not addressed.
	Short-term tests positive for mutagenicity and carcinogenicity in animals and humans for certain extracts of diesel exhaust.	Animal studies data insufficient	Literature reporting no effects from ETS in short-term tests on body fluids neither discussed nor cited.
e. Long-term tests	Addressed	Addressed	Inadequately Addressed
	Notes statistically significant increases in tumors among exposed animals.	Animal studies data insufficient to infer causality	Relevance to inhalation of ETS not addressed.
			Reference to one lung implant study.
f. Human Studies			
Assessment of:			
Adequacy	Addressed	Addressed	Not addressed
	Review & assessment of published stud 5 of 7 case-control studies report statistically signficant increased risks.	Studies inadequate.	No assessment of the studies on spousal smoking and lung cancer in nonsmokers. Critical literature on individual studies not addressed.
Bias	Addressed	Addressed	Inadequately Addressed
	All studies had several limitations, including inadequate characterization of diesel exhaust exposure, lack of validation of surrogate measures of exposure and presence of other confounding factors.		Only one form of bias discussed; recall (exposure) bias not addressed. Did not address inadequate characterization of ETS or lack of validation of surrogate measures.

EPA GUIDELINES	Diesel Emissions	EMF	ETS
Confounders	Addressed	Addressed	Not addressed
	Noted presence of confounding factors	No other agents (confounding factors) have been identified to explain association.	No discussion or citation of studies on confounders re: spousal smoking.
Chance	Addressed	Addressed	Inadequately Addressed
	Evidence for potential carcinogenicity in humans is limited. A few recent studies indicate small but significant risk of lung cancer in occupationally exposed workers. Statistically significant risk of 2.6 reportfor miners & heavy equipment operators.	Association between cancer occurrence & exposure is not strong enough to constitute proven causal relationship largely because the relative risks in published reports have seldom exceeded 3.0 ...	Only 5 studies purported to report statistical significance. All studies used in meta-analysis have relative risks less than 3.0. EPA calculated relative risk of 1.28, based on meta-analysis.
Weight of evidence	Fulfilled	Not fulfilled	Not fulfilled
	Based on limited evidence for carcinogenicity in humans, supported by adequate animal evidence and positive mutagenicity data, diesel emissions considered to best fit weight of evidence category B1.	While some animal tests suggest cancer risk, studies not definitive. This considered a void to be filled before weight of evidence could be completed.	18 of 23 studies fail to achieve statistical significance. Animal inhalation studies not addressed.

EPA GUIDELINES	Diesel emissions	EMF	ETS
DOSE-RESPONSE	Addressed	Addressed	Inadequately Addressed
	Dose-response relationship noted in animal studies.	Inadequate dose-response relationship to infer causality.	States that mainstream and sidestream smoke are qualitatively similar, so ETS is a "lung carcinogen." Later rejects dose-response extrapolation model for active smoking and ETS exposure on the basis that MS and SS differ qualitatively. No actual exposure data considered for estimate of dose.
EXPOSURE ASSESSMENT	Addressed	Addressed	Inadequately Addressed
	Noted that major difficulty w/epidemiologic studies measurement of actual exposure to diesel emissions.	Insufficient basis for postulating human cancer risk from exposure.	No review of actual exposure data on ETS; Use of "spousal" smoking" as the only surrogate measure for exposure; no related discussion regarding questionnaire reliability or recall bias
	Evidence of carcinogenicity considered limited due to lack of actual exposure data on diesel exhaust and other limitations.		Acceptance of cotinine as marker for ETS; no analysis of critical published literature, e.g., studies showing cotinine can arise from non-tobacco sources such as vegetables.

EPA GUIDELINES	Diesel emissions	EMF	ETS
RISK CHARACTERIZATION	Addressed		Inadequately Addressed No application of weight of evidence criteria. Partial review of published extrapolation models for risk estimates on ETS. Risk calculation employed meta-analysis; individual studies were not adjusted for adequacy bias, confounders, or chance. Rejection of linear extrapolation model because it failed to generate appreciable increased risk estimate.
OVERALL CONCLUSION	B1 - Probable human carcinogen	No classification recommended at present	A - Known Human carcinogen

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CRITICISM OF RISK ASSESSMENT GUIDELINES APPLICATION

> "[EPA Administrator William Reilly] said his thinking on [EPA risk assessment policies] is guided in part by the advice he got from Sen. Daniel Patrick Moynihan: 'Above all - above all - do not allow your agency to become transported by middle-class enthusiasm.' 'What he meant,' Mr. Reilly said, 'was "Respect sound science; don't be swayed by the passions of the moment."'"
>
> --The Washington Times, quoting from a speech by EPA Administrator William Reilly

The risk assessment process of the EPA, as well as other government agencies, has come under increasing criticism from:

o legislators

Amendments to the Clean Air Act included:

-- a requirement that the EPA commission the National Academy of Sciences (NAS) to conduct a thorough review (by April 1993) of EPA's risk assessment methodology in determining carcinogenic risk associated with exposure to hazardous toxic chemicals; and

-- created a Risk Assessment and Management Commission to receive and review the report.

o scientists

When the NAS panel on risk assessment, which includes some of the top experts in assessing carcinogenicity of chemicals, held their first meeting, they:

-- stated that they hoped to arrive at "a blue-print for radical reform" to end an outdated risk assessment system;

-- sharply criticized use of MTD testing;

-- criticized regulators for not clarifying that results from animal cancer studies are far from definitive.

Dr. Bruce Ames, head of the biochemistry department of the University of California at Berkeley, was once a proponent of conservative risk assessments. However, he and a number of other scientists now believe that the methods of testing for cancer, rather than the substances themselves, induce high levels of cell division, leading to cancer-causing mutations.

In a 1990 survey of over 1,400 American public health scientists from government, industry and academia, more than 90 percent of the respondents indicated that they believe public health funds in the U.S. are being misdirected by the government. (Source: Carlo et al., "New Science in Risk Assessments," Environmental Claims Journal, Spring 1991)

o the administration

In its "Regulatory Program of the United States Government, April 1, 1990 - March 31, 1991," the Executive Office was highly critical of the present risk assessment process and called on all federal agencies to:

-- ensure that risk assessments are based on current scientific information and realistic assumptions;

-- keep science and policy decisions separate;

-- fully disclose risk assessment limitations to the public.

o the judiciary

Courts repeatedly have found that regulatory agencies must weigh scientific evidence carefully and must take significant new information into account when fashioning rules. In recent cases they have:

-- not allowed agencies merely to assume that no safe levels exist for carcinogens;

-- required hard and realistic evidence of carcinogenicity at low doses, rather than just straight-line models.

o the EPA

-- EPA is considering revisions to its 1986 guidelines;

-- EPA is reviewing its dioxin assessment based on updated scientific research;

-- EPA occasionally uses new evidence and updated methodologies in reviewing or regulating substances.

Science vs. Public Policy

> "EPA's priorities appear more closely aligned with public opinion than with our estimated risk."
>
> --Environmental Protection Agency, "Unfinished Business," a ranking by EPA staff of 31 environmental problems (1987)

A major concern about the government risk assessment process is the difficulty of keeping risk management and risk assessment separate.

According to the Office of Management and Budget's "Regulatory Program, April 1, 1990 to March 31, 1991" continued problems with separating science and policy decisions are exacerbated by:

- continued reliance on conservative (worst-case) assumptions, which distort risk assessment;
- conservative biases embedded in various stages of risk assessment, which impart a substantial margin of safety; appropriate margin should be determined by risk management officials, not be pre-empted in biased risk assessments;
- conservatism in risk assessment, which distorts regulatory priorities by directing resources to reduce trivial carcinogenic risks, rather than addressing more important risks.

Specific concerns raised with respect to the risk assessment procedure are outlined below:

Procedure	Problem	Example
Scientists' reliance on genetically sensitive test animals.	It is unclear that these species accurately mimic biological responses in humans.	One-third of a common test species spontaneously develop liver tumors. Despite questions about reliability of data using such species, cancer risk assessments often proceed on the assumption that these data are sufficient to conclude a substance is a carcinogen.
Consideration of all relevant studies.	Studies that indicate a statistically significant positive relationship routinely receive more weight than studies indicating no relationship at all.	Alar received "probable human carcinogen" classification based on a single positive animal bio-assay. 3 high-quality negative studies showed no significant effects; they received little or no weight in the classification decision.
Risk-assessment guidelines generally give greatest weight to the most sensitive animals.	If substance is found to cause cancer in one species or gender but exhibits no effects elsewhere, results pertaining to the sensitive species typically are used to develop estimates of human health risks.	If male mice develop cancer from substance, but female mice and rats of of both genders do not, results from the male mouse often will be used to derive estimates of cancer risks to humans.
Use of Maximum Tolerated Dose (MTD) procedure -- Administering the largest dose possible without killing the test species.	High doses can be toxic for reasons unrelated to their capacity to cause cancer.	Formaldehyde causes nasal tumors in rats under MTD. It is unclear whether the cancers are induced by formaldehyde or toxic effects of high doses.

Procedure	Problem	Example
Consideration of species-specific characteristics when evaluating significance of animal data.	Species-specific characteristics often neglected when guidelines applied to specific substances. Assumption made that animal data can be meaningfully extrapolated to humans.	Study of chemicals under U.S. National Toxicological Program reported assumption of meaningful extrapolation can lead to erroneous classification as many as 27 out of 100 chemicals as probable human carcinogens.
Conversion from test animals to humans	Approach used by EPA leads to estimates of risk between 7 and 12 times greater than FDA.	EPA estimates of cancer risk from formaldehyde, benzene or pesticides are roughly 10 times higher than FDA's.
Use of Worst-Case Environmental Conditions	Data from unusually sensitive or highly contaminated environments projected to develop general national estimates of health risks generally result in misleading and unreliable estimates.	
Use of the Maximum-Exposed Individual (the person whose exposure is greater than all others)	Estimates to entire population may be based on upper-bound cancer risk to MEI, resulting in risk estimates substantially higher than actual risk.	For radon exposure, EPA calculates exposure of hypothetical person who lived right outside source (uranium mine vents), and never strayfrom that spot for 70 years.
Use of Assumptions rather than real-world exposure data	Models overstate exposure resulting in substantial overstatement of risk.	EPA reduced its upper-bound lifetime cancer risk for pesticide Captan by two orders of magnitude (20 times) when it replaced original assumptions with real-world data.

Procedure	Problem	Example
Assumption that there is no safe level of exposure for carcinogens.	Models assume that exposure to even one molecule of a carcinogen poses some risk of cancer.	Based on this assumption, dioxin was labeled as the most potent cancer-causing chemical known to man. A recent meeting of scientists at the Banbury Center of the Cold Spring Harbor (Oct. 21-24, 1990) reached the conclusion that there probably is a "safe" level of dioxin. EPA is now undertaking a reassessment of dioxin. (Source: Inside EPA)
Assignment of a single number risk value for alleged carcinogens.	EPA risk value for carogens is presented as a single number. Although there is boilerplate language that the actual risk is likely to be lower than stated and may even be zero, this information is rarely communicated to policy-makers or the public by the agency.	
Improper prioritization of risks	EPA has been overemphasizing trivial cancer risks while ignoring larger risks.	A recent SAB report called for risk-based prioritization, with greater emphasis on ecological risks and reducing lead. (Source: Inside EPA)

Procedure	Problem	Example
Continuing risk assessments while the EPA risk assessment process is reviewed.	EPA has been inconsistent continuing with some risk assessments and putting others on hold while its risk assessment process undergoes an in-depth review internally and by the National Academy of Sciences, with potential for major revision.	Perchloroethylene, a widely used dry cleaning solvent, is under review for possible upgrading of its EPA classification. EPA's review is being stalled due to the NAS review, so that agency revisions coincide with NAS recommendations. However, other agents which could be as significantly affected by revisions to the EPA risk assessment process are being pushed through. (Source: Inside EPA)

(Source for examples, unless otherwise noted: Office of Management and Budget, "Regulatory Program, April 1, 1990 to March 31, 1991")

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Precedence

"There is not much precedence in the Federal establishment for pulling back from a judgment of toxicity. But we need to be prepared to adjust, to raise or lower standards, as new science becomes available."

--EPA Administrator William Reilly, New York Times (8/15/91)

Past and present EPA actions and procedures have resulted in the following questionable policy decisions, among others.

o Dioxin

Background:

In 1983, dioxin was characterized as the most dangerous known human toxin. The town of Times Beach, Mo., was abandoned due to dioxin found in dirt roads, and the government orders an expensive clean-up effort, funded by the government and Syntex, the company deemed responsible for the contamination.

In August 1991, EPA, U.S. Surgeon General and the Centers for Disease Control announced that new scientific data indicated a lower level of risk should be assigned to dioxin. Dr. Vernon Houk, the federal scientist who ordered the evacuation of Times Beach, said: "If it's a carcinogen, it's a very weak carcinogen, and Federal policy needs to reflect that."

Result:

Over $100 million already spent on clean-up effort. Estimated that total cost will reach $290 million. Legislation passed this year requires the Department of Veterans Affairs to pay disability benefits to soldiers who can prove they were exposed to dioxin in the form of Agent Orange and suffer from chloracne and certain lymphomas and soft-tissue sarcomas.

(Source: The New York Times, 8/15/91)

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o Alar

Background:

In 1989, the Natural Resources Defense Council labeled Alar, a growth agent for apples, as "the most potent cancer-causing agent in our food supply ... as many as 5,300 children may contract cancer from their preschool exposure."

Meryl Streep testified on behalf of the NRDC on Capitol Hill. "60 Minutes" did a segment on the alleged dangers of Alar.

Although the EPA felt NRDC was overstating the danger, EPA gave Alar a Group B carcinogen classification -- based on one discredited, positive study. EPA gave little weight to 3 high-quality negative studies and recommended a ban. Producer voluntarily withdrew Alar from market.

Result:

Apple growers lost an estimated $100 million and dozens of family-owned orchards were forced into bankruptcy.

o EDBs

Background:

Ethylene dibromide (EDB) was banned by EPA, based on conservative risk assessment. The grain and soil fumigant combats vermin and molds -- vermin transmit disease, and molds harbor the natural potent carcinogen aflatoxin B.

The estimated human cancer risk from aflatoxin in one peanut butter sandwich is about 75 times greater than a full day's dietary risk from EDB exposure (Source: Dr. Bruce Ames, University of California at Berkeley).

Result:

Higher food prices, lost commodities of over $2 billion per year, and potentially greater risk to consumers. By eliminating the relatively small hazard from EDB, federal risk managers may have intensified the relatively potent threat of aflatoxin associated with an increase in mold contamination.

o Radon

Background:

EPA has released several warnings on radon to the public and released a draft "Citizens' guide to radon: don't let this dangerous intruder invade your home," that states that millions of homes may be at or above the reference level of concern (4 picocuries/liter). EPA also has stated that as many as 20,000 people may die each year from cancer caused by radon.

Although most scientists concede that radon can be extremely hazardous, "a number of scientists have bluntly criticized EPA's office of radiation programs for exaggerating the risks posed by indoor radon exposure and using scare tactics to frighten the public into conducting radon tests on their houses."

"'The scientific community continues to be dumfounded [sic]' by EPA's focus on 'average' radon levels, [Anthony] Nero [senior scientist for the indoor environment program at the Lawrence Berkeley Laboratory] notes."

Scientific community also takes issue with how radon measurements are taken, and that EPA reference levels are based on studies of miners.

(Source: Inside EPA, 11/9/90)

Result:

At least 8 House and Senate measures related to radon. Use of unrealistic assumption that individuals live at the point of maximum exposure for 24 hours a day, every day for 70 years generates fears and "radon hysteria." Unrealistically low levels of reference have negatively impacted homeowners, businesses, education and health-care facilities.

(Sources: "Some Scientists Say Concern Over Radon Is Overblown by E.P.A.," The New York Times, 1/8/91; "Thumbs on the scales of risk?" The Washington Times, 3/12/91; Inside EPA, 11/9/90)

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o Electro-magnetic Fields

Background:

In 1990, the EPA prepared a preliminary draft report on EMFs that reported that certain magnetic fields were a "probable, but not proven," cause of cancer in humans. Several weeks later, the report was reivsed, downgrading the hazard to a "possible" cause of cancer.

The committee appointed by the EPA's Science Advisory Board reviewed the EPA report. Additionally, the White House science office set up a special committee to review the report.

Result:

Independent committee met in public sessions and listened to wide-ranging views. The panel found the EPA report seriously deficient and recommended that it be completely re-written and re-reviewed. White House committee also found report deficient.

(Source: Inside EPA)

o Asbestos Removal

Background:

In the early 1970s, the EPA added asbestos to its list of hazardous materials, and restricted its use in building products. However, EPA failed to set clear rules for determining when asbestos-containing materials in buildings may pose risks. Scientists dispute EPA's position that a visual inspection is sufficient to determine if asbestos abatement is required in a building, believing that air monitoring is more accurate.

In addition, in 1986, Congress passed legislation for EPA to regulate asbestos-containing materials in public and private schools.

Result:

EPA's actions touched off a wave of panic that has cost taxpayers billions and may have done nothing to improve the situation. In 1988, EPA admitted that asbestos removal is not always the best solution, but only after thousands of schools and office buildings may have been needlessly ripped apart,

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displacing students and office workers alike. Also, "rip and skip" asbestos abatement operations have sprung up, often leaving an asbestos site more dangerous than before.

On October 21, 1991, the 5th Circuit Court of Appeals threw out a 1990 ban by the EPA on importing, making or using asbestos, saying the EPA didn't give opponents of the rule a chance to make their case. (Source: The Washington Post, 10/22/91)

o PCBs

Background:

Polychlorinated biphenyls (PCBs) were developed in the 1920s. Their major use has been in electrical equipment (transformers and capacitors) where their important electrical insulating properties reduced the hazard of fire and explosion.

In the 1970s, two incidents made PCBs the most prominent chemical material used to promote the Toxic Substances Control Act being considered by Congress: 1) trace quantities were found to be widely distributed in the environment and were believed to be harmful to wildlife, and 2) approximately 1,000 persons became ill after an accidental leakage into rice oil being processed for cooking use in a Japanese plant.

Despite substantial scientific review and government reports that basically cleared PCBs as toxic substances, they were restricted under the Toxic Substances Control Act and were rated as a "probable human" carcinogen by the EPA.

They were described in the media as "a class of chemicals ... linked to cancer and birth defects, water pollution and wildlife contamination," even though scientific evidence does not necessarily support that reputation.

Result:

EPA presently is considering a request to re-evaluate its cancer risk assessment for PCBs based on new studies that show some forms of the chemical to be less hazardous than currently believed. Although the EPA may not reconsider its risk assessment at this time, an EPA source said that sooner or later a review would be unavoidable because of the intense research efforts focused on PCBs.

(Sources: Edward J. Burger, Jr., "Health as a Surrogate for the Environment," Daedalus, Fall 1990; Inside EPA, 7/26/91)

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PUTTING RISK INTO PERSPECTIVE

"--Scientists have gotten better at finding possible carcinogens in extremely small amounts, such as one-trillionth. One part per trillion is like one dollar to the federal budget, or six inches in the distance to the sun. Increasingly, the public and media have to judge what amounts are being talked about when things are labeled carcinogenic."

--"Confusion Persists over Health Risks," The Seattle Times, 9/25/91

The word "carcinogen" can strike fear into the heart of almost anyone. However, because we are able to measure the presence of carcinogens and purported carcinogens in such miniscule amounts, we tend to believe the mere presence of such a substance indicates a high risk.

This type of thinking, along with conservative risk assessment, can distort our perception of true risk.

Carcinogens As Part of Everyday Life

"Ames and Gold estimate that plant foods contain 5,000 to 10,000 natural pesticides and break-down products. ... Compared to the amount of synthetic pesticides we consume, we eat about 10,000 times more of the plant pesticides."

--Philip H. Abelson, Deputy Editor, "Testing for Carcinogens with Rodents," Science, 9/90

We are exposed to suspected carcinogens in our food and water on a daily basis. The following chart illustrates our everyday exposure to carcinogens, many of which occur naturally.

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■ AFLATOXINS
Exposure
grains
peanuts
tree nuts
cottonseed meal
meats
eggs
milk

■ ARSENIC AND CERTAIN ARSENIC COMPOUNDS
Exposure
drinking water
tissue of livestock

■ BENZENE
Exposure
drinking water
fruits
fish
vegetables
nuts
dairy products
eggs

■ VINYL CHLORIDE
Exposure
drinking water

■ ACETALDEHYDE
Exposure
milk products
baked goods
fruit juices
candied desserts
soft drinks
synthetic flavoring ingredient to impart orange, apple, and butter flavors
vinegar
yeast
fruit and fish preservatives
all ripe fruits
mustard
cooked beef and chicken

■ CHLOROFORM
Exposure
drinking water
seafood
dairy products
meats
oils/fats
vegetables
breads

■ DIBROMOETHANE (Ethylene Dibromide)
Exposure
potatoes
vegetables
fruits
pineapples
cotton
tobacco
peanuts
fruit trees

■ ETHYLENE OXIDE
Exposure
dairy products
spices
black walnuts
copra
cocoa
bleached, wheat? flour
dried fruits
dehydrated vegetables
fish
bone meal
beer
food additives

■ FORMALDEHYDE (GAS)
Exposure
plants
maize leaves

■ LINDANE AND OTHER HEXACHLOROCYCLOHEXANE ISOMERS
Exposure
milk
eggs
dairy products
seafood

■ N-NITROSODIETHYLAMINE
Exposure
drinking water
cheeses
soybeans
soybean oil
various fish
salt-dried fish
cured meats
alcoholic beverages

■ N-NITROSOPYRROLIDINE
Exposure
fried bacon
spices

■ OCHRATOXIN A
Exposure
corn
peanuts
storage grains
cottonseed
wheat
maize
rye
barley
oats
peanuts
coffee beans
breads
bleached, wheat? flour
rice
peas
beans
beer

■ POLYCYCLIC AROMATIC HYDROCARBONS
Exposure
smoked, barbecued, or charcoal-broiled foods
vegetables
vegetable oils
margarines
roast coffee
coffee powders
fresh sausages
cereals
grains
bleached, wheat? flour
breads
meats
seafood
fruits
processed foods
water (drinking, fresh, sea)

■ SACCHARIN
Exposure
dietetic foods
dietetic drinks
toothpastes
mouthwashes

■ SAFROLE
Exposure
spices (particularly nutmeg and mace)

■ 2, 3, 7, 8-TETRACHLORODIBENZO-P-DIOXIN (TCDD)
Exposure
root vegetables
fish
meats
milk

■ URETHANE
Exposure
wine
beer
orange juice
some soft drinks
ale
breads
soy sauce
yogurt
olives

(Source: "Sixth Report on Carcinogens 1990," the U.S. Department of Health and Human Services)

Putting Animal Tests into Perspective

> "The principal method of determining potential carcinogenicity of substances is based on studies of daily administration of huge doses of chemicals to inbred rodents for a lifetime. Then by questionable models ... results are extrapolated to effects of miniscule doses in humans. Resultant stringent regulations and attendant frightening publicity have led to public anxiety and chemophobia.
>
> --Philip H. Abelson, Deputy Editor, "Testing for Carcinogens with Rodents," Science, 9/90

The design and interpretation of animal studies for regulatory action and public health also is controversial. One of the main controversies concerns the usage of MTD -- maximum tolerated dosage -- methodology, whereby the scientist typically feeds the lab animals the highest possible dosage the animal can ingest without dying of toxic poisoning. The results of these tests are then extrapolated to determine the potential effect of the substance on humans. These results generally are taken into consideration by the EPA when setting guidelines.

One of the strongest criticisms of this methodology is that there is evidence that lab animals may be developing tumors from amount of the substance they are force-fed, as opposed to developing tumors from the substance itself.

The following table compares actual dosages of alleged carcinogens fed to test animals and the equivalent of those substances for humans.

TABLE II: COMPARATIVE ANIMAL/HUMAN DOSES FOR SELECTED CHEMICALS[28]

CHEMICAL	EXPERIMENTAL DAILY DOSE (RODENTS UNLESS NOTED)	EQUIVALENT HUMAN INTAKE
Cyclamates	5% in diet (2.18 gms/day)	138-522 12 oz. bottles of soda (daily) or about 80-240 times typical human intake.
Saccharin	0.5, 5.0, or 7.5% in diet (a)	40-400 times daily human intake or up to 500 times typical consumption of sweeteners (b)
DES	One clinical treatment (c)	5 million pounds of beef liver from treated cattle for 50 years
Safrole	5,000 ppm in diet (0.5%)	613 12 oz. bottles of root beer daily
Alar (d)	5,000-10,000 ppm in diet (0.5 to 1.0%)	28,000 pounds of apples daily for 10 years

Notes:

(a) Only a few bladder tumors found for high dose animals. European studies[2] at 0.5% intake produced no tumors.

(b) Average sugar consumption is about 150 grams per day. A saccharin dose of 3.75 mg. per day per kg. body weight is equivalent to the sweetness of 135 kg. of sucrose or sugar per day.

(c) The experimental dose refers to the clinical DES dose to women, not an animal dose.

(d) Alar (daminozide) is a plant growth regulator that improves apple texture, appearance, crispness, and storage characteristics.

(Source: American Council on Science and Health, from a study by H.F. Kraybill, "From Mice to Men: Predictability of Observations in Experimental Systems and Their Significance in Man."

Putting Epidemiology in Perspective

"It is important to remember the pitfalls in interpreting [epidemiologic studies] and to be cautious in advising patients on the basis of single or conflicting studies. This is particularly true of studies that purport to show only weak associations between exposure and disease."

--Marcia Angell, M.D., executive editor, New England Journal of Medicine, "The Interpretation of Epidemiologic Studies," NEJM, 9/20/90

"[Physician-author] Lewis Thomas has suggested that epidemiologic studies of noninfectious disease have produced their own adverse side effect: an 'epidemic of apprehension.'"

--Dr. Alvan Feinstein, director, Clinical Epidemiology Unit, Yale University, "Scientific Standards in Epidemiologic Studies of the Menace of Daily Life," Science, 12/88

The design and interpretation of epidemiologic studies for regulatory action and public health is controversial. Use of such studies is limited, especially when the relative risk is low, i.e., when the reported association is weak. Factors such as bias and confounders can impact the results, creating the impression of an association between a substance and effect when in fact, none exists.

To put it into perspective, the following table shows the relative risk attributed to certain substances for a given effect based on epidemiologic studies. All of the following studies report a weak association, and all of the studies report a relative risk higher than the 1.28 attributed to ETS by the EPA in its meta-analysis.

Risk Factor	Health Outcome	Estimate Of Relative Risk	Reference
Emergency room visit in 3 years prior to diagnosis (< 45 years)	Cervical cancer, invasive	1.63	Celentano, et al. J Clin Epidemiol 1988; 41(6)
Mother aged 20-24 yrs. father aged 30-34 yrs. at daughter's birth	Breast cancer in adult daughter	1.84	Janerich, et al. Clin Epidemiol 1989; 42(2)
Migraine headaches common type	Ischemic stroke	1.3	Henrich et al. J Clin Epidemiol 1989 42(8)
Age 30-31 yrs. at first full-term pregnancy	Breast Cancer	1.41	Layde, et al. J Clin Epidemiol 1989; 42 (10)
Electric blanket use	Nonseminoma tumor	1.4	Verreault, et al., Am J Epidemiol 1990 131(5)
Women who used semi-permanent hair dye between 1-9 times	Breast cancer	1.3	Koenig, et al. Am J Epidemiol 1991; 133 (10)
Employment in schools	Bladder cancer	1.4	Vineis, et al., Int. J Cancer 1985; 35
Consumption of carrots, women	Breast cancer	1.71	Hisop, et al. Am J Epidemiol 1990; 131 (2)
Frequent consumption of fruit sources high in vitamin A, women	Breast cancer	1.49	Hislop, et al. Am J Epidemiol 1990; 131 (2)
User of Vitamin B supplements, women	Breast cancer	2.07	Hisop, et al. Am J Epidemiol 1990; 131 (2)
Top socioeconomic status	Mortality (lymphoma, myeloma)	1.4	Pearce et al. Am J Epidemiol 1985, 121 (2)

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Risk Factor	Health Outcome	Estimate Of Relative Risk	Reference
Carbohydrates	Stomach cancer	1.5	Risch, et al., Am J Epidemiol 1985; 122 (6)
Eggs	Mortality (female)	1.3	Kahn, et al., Am J Epidemiol 1984; 119 (5)
Pepper	Mortality (both sexes	1.3	Kahn, et al., Am J Epidemiol 1984; 119 (5)
Height <59 inches (women)	Myocardial infarction	1.5	Palmer, et al. Am J Epidemiol 1990; 132(1)
Firefighters in Washington state	Tumors of brain and CNS tumors	1.80	Howe and Burch; Am J Epidemiol 1990 132(6)
Parents married, Sweden	Inflammatory bowel	1.6	Ekbom, et al. Am J Epidemiol 1990; 132 (6)
High intake of iron males	Rectal cancer	2.15	Freudenheim, et al. Am J Epidemiol 1990 131(4)
High protein intake males (Utah)	Colon cancer	2.5	West, et al. Am J Epidemiol 1989; 130 (5)
Low beef consumption (Canada)	Melanoma	1.5	Gallagher, et al. Rec Results Cancer Res 1986; 102
Exposure to floure-scent light between 10-19 years, women	Melanoma	2.5	Elwood, Rec Results Cancer Res 1986; 102

PART II

8

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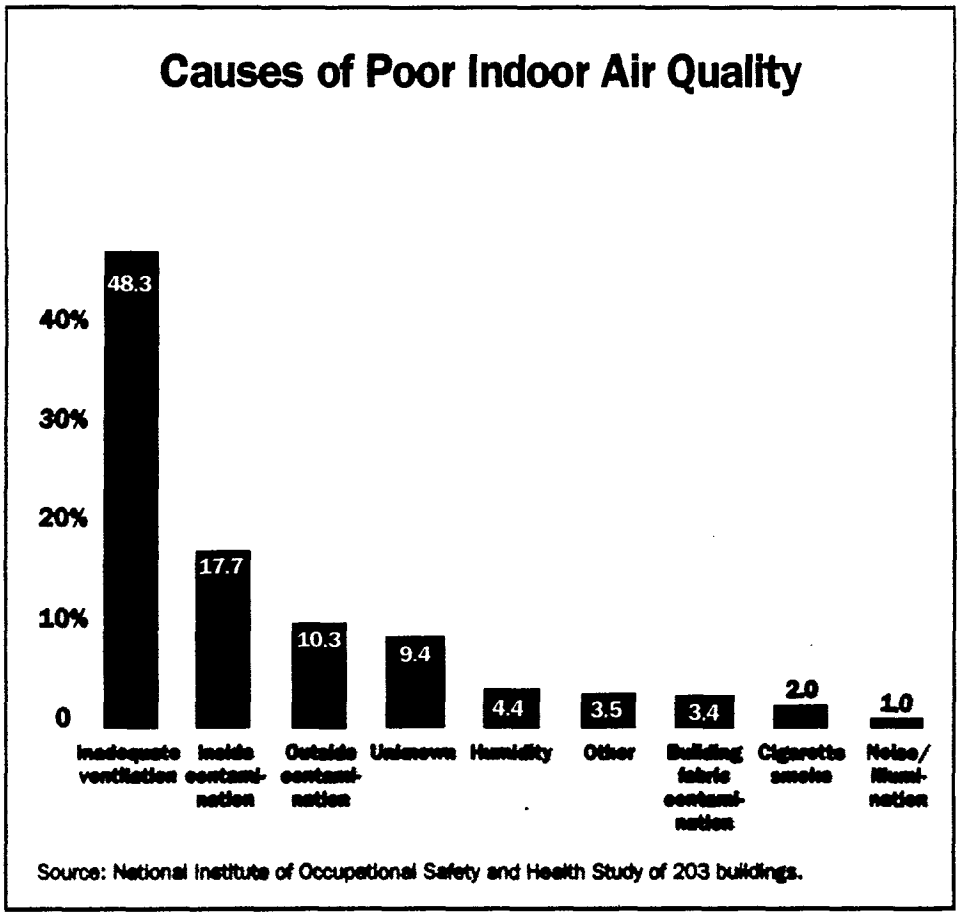
POOR INDOOR AIR QUALITY AND "SICK BUILDING SYNDROME"

Extensive research by governmental agencies and private organizations on "sick buildings" in the United States, Canada and Europe has demonstrated that the overwhelming majority of problems with poor indoor air quality, or "sick-building syndrome," result from a combination of too many impurities and too little ventilation.



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- A study of more than 200 sick buildings by the National Institute for Occupational Safety and Health (NIOSH) reported ETS as a source of claimed discomfort in only 2% of buildings.

- Air quality tests in 26 schools with elevated radon levels revealed that all the schools had ventilation problems. One author of the study, which was organized by EPA, stated that most air quality problems can be eliminated when ventilation systems are functioning properly.

- Eight workers in the EPA's headquarters building in Washington, D.C., filed suit against the owner and building manager alleging neglect to take reasonable steps to ensure adequate air quality. They assserted that a "sick building" problem had arisen from disruption of the building's ventilation system during renovation, allowing chemicals to continuously circulate. It is a non-smoking building.

- A study of 412 sick buildings from 1981 to 1988 reported ETS as a significant concern in only 3% of buildings (Robertson, 1990).

- A study of 408 sick buildings reported ETS as a significant factor in less than 3% of the buildings (Collett, 1989).

Causes of sick-building syndrome:

- Poor ventilation and poorly maintained ventilation systems from dirt and corrosion or closed air-intake dampers.

- Inadequate filtration.

- Contamination from bacteria, molds and fungi.

ETS is often blamed for indoor air quality problems because:

- It is visible

- It is easily identifiable by its odor

In fact, because ETS is the most visible air factor, it is often the first signal that ventilation systems are not working properly.

Ventilation

> "ASHRAE's 1981 standard meant that tobacco smoke had inadvertently become the benchmark of the adequacy of ventilation. Smoke tubes have been used for many years to test ventilation systems and trace air distribution. In such tests, if the ventilating system is incapable of dealing with smoke, it is also incapable of dealing with other invisible pollutants. But if smoke is the most important criterion in setting ventilation rates, indoor air quality is bound to suffer."
>
> --P. Binnie, "The Role of Ventilation in Controlling the Quality of Indoor Air, Including ETS"

In 1981, the American Society of Heating, Refrigeration and Air-Conditioning Engineers (ASHRAE) issued a ventilation standard for public places, ASHRAE 62-1981, which recommended two levels of ventilation:

- smoking areas (20 cubic feet per minute/person)
- non-smoking areas (5 cubic feet per minute/person)

In 1989, ASHRAE issued a revised ventilation standard of 15-20 cubic feet per minute/person for all public places (ASHRAE 62-1989) because further research had shown:

- the non-smoking ventilation rates were insufficient to remove some constituents of poor indoor air quality; and
- separate ventilation standards are not required based on the presence of smokers.

The new standard serves as a guide for:

- preventing indoor air problems;
- establishing ventilation rates for indoor areas to "control carbon dioxide and other contaminants with an adequate margin of safety, and to account for variations among people, varied activity levels, and a moderate amount of smoking."

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The new standard has been approved by the American National Standards Institute, and is expected to be adopted by the major building code organizations in the United States. The standard then will become part of the building codes used by local governments and municipalities.

Cost

"Cost is a consideration which will reduce the effectiveness of a ventilation system. Bringing in more fresh air is no doubt more expensive to heat or cool than simply recycling the air, however, these costs can be offset by the reduction in indoor air quality problems. Employee absenteeism, complaints and even litigation can be very expensive and quite preventable. In the long run a properly run ventilation system is most cost effective."

--H. Goodfellow and J. Wyatt, "Critical Review of Ventilation Contaminants in Indoor Air"

Researchers have estimated that increases in operating costs under the standard could run as low as 3 percent.

However, a number of researchers agree that increased worker absenteeism attributable to poor indoor air quality would greatly exceed any increased energy expenditures due to ASHRAE 62-1989:

- A 1 percent absenteeism rate (attributable to poor indoor air quality) would equal an expenditure of $100,000 over the year compared to an increased annual cost for ventilation of $20,000. (P. Binnie, "The Role of Ventilation in Controlling Poor Indoor Air Quality.")

- For a 100,000 sq. foot office building, increased energy costs for an entire year would equal only one-half day of absenteeism spread over the entire building's workforce. (R. Miller, Indoor Air Quality)

- Energy can be assumed at around $3.00/sq. ft./year and human capital can be assumed at as much as $300/sq. ft./year. Even a dramatic change of 25%-50% of energy costs would equal only a few minutes of human capital time or productivity. (H. Goodfellow and J. Wyatt, "Critical Review of Ventilation Contaminants in Indoor Air")

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Other Processes

Two other processes also been used to achieve acceptable indoor air quality, but have limitations that can be serious:

- **filtration and air cleaning** -- cleaning and filtration of outdoor supply air and air that is recirculated within an occupied space.

  Limitations: If filters are of poor quality or low efficiency, or are not changed with recommended frequency, the purpose is defeated and filtration may exacerbate an indoor air quality problem.

- **source control** -- removal of a substance reportedly linked with complaints about indoor air quality.

  Limitations: Removal of a substance thought to be causing a poor indoor air quality does not guarantee acceptable indoor air, because it does not necessarily address the root of the problem, e.g., inadequate ventilation.

  Example: When a major Virginia financial institution began receiving employee complaints related to poor indoor air quality after moving into a new building, it banned smoking. A comprehensive examination showed the real culprits to include: sealed fresh-air intakes; cheap panel filters; ductwork internally coated with mold and mildew of known allergens; and carbon dioxide levels 5 times greater than outdoors.

Separation of Smokers and Nonsmokers in the Workplace

> "The results indicate that the provision of a designated, but no separately ventilated smoking area can effectively eliminate or drastically reduce most components of environmental tobacco smoke from nonsmoking offices."
>
> --T. Sterling and B. Mueler, "ETS in Offices and When Smoking is Restricted to Designated but not Separately Ventilated Areas," Indoor Air Quality, 1990.

There has been argument that ventilation is not effective in diluting ETS and that simply separating smokers and nonsmokers in the workplace does not minimize nonsmoker exposure to ETS. However, recent studies reported:

- use of designated smoking areas reduced ETS by 95 percent.
- ambient nicotine in nonsmoking areas was virtually undetectable, suggesting that ETS had a negligible impact on the nonsmoking areas of the building.
- no significant differences in average ETS constituent levels between nonsmoking offices that received air recirculated from designated smoking areas and nonsmoking offices that did not receive such recirculated air.

Workplace Policy Guidelines

The EPA has addressed the matter of ETS in the workplace by issuing a draft workplace policy guide recommending that ETS be eliminated in the workplace and public facilities.

This draft workplace policy guide was issued concurrently with the EPA's draft risk assessment on ETS.

- The workplace guide was based on conclusions reached in the draft ETS risk assessment, and provided guidelines based on science that had not been reviewed, causing speculation that the agency had predetermined its stand on ETS.

- Most of the science used in the ETS risk assessment, and on which the workplace policy guideline was based, does not address ETS in the workplace. The 11 studies which did address ETS in the workplace showed no increased risk of lung cancer due to exposure.

- EPA has no authority to regulate health and safety matters in the workplace; that falls under the aegis of the Occupational Safety and Health Administration (OSHA).

- On Sept. 20, OSHA published a request for information on indoor air to determine whether measures are necessary to ensure better indoor air quality in the workplace.